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Poly is more Effective than Mono - Unsaturated Fat For dietary management IN the Metabolic Syndrome: The MUFFIN Study

Michael Miller, MD[*,1,2,3,5,6], **John D. Sorkin, MD, PhD**[1,4,5,6], **Laura Mastella, DNP**[1,4,5], **Aimee Sutherland, BA**[5], **Jeffrey Rhyne, BA**[1,3], **Patrick Donnelly, BA**[1], **Kathy Simpson, RD**[1,4,6], and **Andrew P. Goldberg, MD**[1,4,5,6]

[1]Department of Medicine, Baltimore, MD

[2]Department of Epidemiology and Public Health, Baltimore, MD

[3]Division of Cardiology, Baltimore, MD

[4]Division of Gerontology and Geriatric Medicine, Baltimore, MD

[5]University of Maryland School of Medicine, Baltimore, MD

[6]Geriatric Research Education and Clinical Center, Veterans Affairs Medical Center, Baltimore 21201.

Abstract

Background—The Metabolic Syndrome (MetS) is highly prevalent and associated with an increased risk for Type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD). Lifestyle recommendations to treat MetS often include the replacement of saturated fats (SFA) and monosacharides with unsaturated fat. However, it is unclear whether metabolic parameters will improve more when the saturated fat in American Heart Association (AHA) diets is replaced with higher concentrations of mono or poly-unsaturated fatty acids (MUFA, PUFA).

Objective—To test the hypothesis that an AHA diet enriched in MUFA improves lipoprotein lipids, insulin resistance, inflammation and endothelial function to a greater extent than a diet enriched in PUFA in middle-aged men and women with MetS.

Methods—A prospective, open-label, parallel group design with randomization to a hypocaloric MUFA or PUFA enriched diet following weight stabilization on an AHA Step I diet. Participants consumed 3 MUFA or PUFA enriched muffins daily with additional supplementation as required to ensure 25-50% increases in dietary fat intake from these sources at the expense of SFA and the

[*]To whom correspondence should be addressed: 110 S. Paca St, Suite 7-124, Baltimore, MD 21201, Office: (410) 328-6299, Fax: (410) 328-3530, mmiller@medicine.umaryland.edu.

Author Contributions: MM and APG were involved in all aspects of the study, including designing the study, writing the manuscript and data analysis and interpretation; JDS was involved in analyzing and interpreting the data and writing the manuscript. LM, JR, PD were involved in the clinical and technical aspects of the study. AS and KS were involved in nutrition and food record analysis.

Conflicts of Interest.

There are no conflicts of interest for any of the authors.

opposing unsaturated fat. Changes in MetS components were measured at baseline and after 6 months of dietary intervention.

Results—Thirty-nine participants (mean age 60.8 years, 79% African-American, 60% women) with MetS completed the 6-month study. Compared to baseline, assignment to either MUFA (n=23) or PUFA (n=16) both were associated with weight loss (WL) (MUFA: −2.3±1 kg, *P=0.06*; PUFA: −4.6±2 kg; *P=0.002*), but PUFA was also associated with reductions in triglycerides (TG) (−30±18 mg/dL, *P=0.02*), systolic blood pressure (BP) (−7±3 mmHg, *P=0.01*), diastolic BP (DBP) (−4±2 mmHg, *P=0.01*) and improved flow mediated dilation (FMD) (7.1±1.8% vs. 13.6±2%, absolute increase; *P=0.0001*). When compared to MUFA treatment, PUFA intervention was associated with reduced TG (*P=0.04*) and DBP (*P=0.07*) as well as increased FMD (*P=0.04*) even after adjustment for changes in weight. There was no effect on total cholesterol, low-density lipoprotein cholesterol (LDL-C), glucose, high-sensitivity C-reactive protein (hs-CRP) or other inflammatory proteins. Overall, 25% (4 of 16) assigned to PUFA and 13% (3 of 23) to MUFA converted to non-MetS status.

Conclusion—Substitution of SFA with PUFA in patients with MetS is associated with greater reductions in TG and improvement in endothelial function than MUFA that is independent of WL. These preliminary findings raise the possibility that PUFA may be the unsaturated fat of choice to reduce cardiometabolic risk in patients with MetS.

Introduction

The Metabolic Syndrome (MetS) is a common condition characterized by three or more of the following metabolic abnormalities: (1) blood pressure (BP) ≥130/85 mmHg, (2) fasting glucose ≥100 mg/dL, (3) waist circumference ≥ 102 cm (40 inches) in men and 88 cm (35 inches) in women and dyslipidemia (4) (triglycerides [TG] ≥150 mg/dL and (5) high-density lipoprotein cholesterol [HDL-C]< 40 in men and <50 mg/dL in women). The metabolic syndrome is associated with an increased risk of Type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) (1,2). While lifestyle modification (changes in diet and increased activity) is the cornerstone of initial therapy in MetS, the most beneficial dietary measures to reduce weight and improve the associated abnormal metabolic characteristics of the MetS remains unclear. After early studies identified a high intake of saturated animal based-fat to be associated with increased risk of CVD (3-7), a shift to higher carbohydrate (CHO) combined with lower total and saturated fat acid (SFA) intake was advocated by the American Heart Association (AHA) (8). However, because high CHO diets enriched with monosaccharides were associated with worsening of metabolic parameters, especially in subjects with obesity and T2DM, the scientific sentiment shifted in favor of substitution of unsaturated fat (9). Unsaturated fats are divided into two types, mono- and polyunsaturated fats. However, the optimum type of fat to consume remains controversial. For example, higher intake of monounsaturated fatty acids (MUFA) has been associated with reduced CVD risk in some studies (10-11), whereas other studies identified polyunsaturated fatty acids (PUFA) to be more strongly cardioprotective (12-13). Intake of MUFA or PUFA has been shown to reduce inflammation (14,15) although it is suggested that MUFA may be more potent than PUFA at reducing oxidation of LDL particles (16) and decreasing platelet aggregation (17). Moreover, a MUFA enriched Mediterranean diet is associated with

reduced incidence of MetS and components of MetS (18), as well as excellent adherence rates (19). Thus, a MUFA enriched diet may be the most acceptable diet for MetS, from both a biochemical and adherence standpoint. Yet, few if any studies have directly compared a hypocaloric AHA diet enriched in MUFA or PUFA and lower in SFA on the metabolic abnormalities associated with MetS. This is an important clinical issue because long-term improvement in these metabolic parameters might translate into reduced risk of CVD complications associated with MetS. We hypothesized that a MUFA rather than a PUFA-enriched AHA diet combined with weight loss (WL) would be associated with greater cardiometabolic benefits of MUFA as compared to PUFA in overweight subjects with MetS.

Materials and Methods

Adult men and women with MetS were recruited from the Baltimore VA Medical Center, University of Maryland Medical Center and local hospital outpatient general medicine clinics. Inclusion criteria permitted the use of medication for hypertension (HTN) and type 2 diabetes mellitus (T2DM) (e.g., oral hypoglycemic agents), provided that the medication dosage regimen was stable for a minimum of three-months prior to study entry. Exclusion criteria included subjects with T2DM treated with insulin, hemoglobin A1C >9% or untreated metabolic (e.g, thyroid, Cushing's) disorders. The study was designed to measure several different CV risk-associated parameters including 1) biochemical measurements (e.g., lipoprotein lipids, glucose, insulin, biomarkers of inflammation), and 2) physiological assessment of endothelial function using brachial artery reactivity testing (BART) (20). **Figure 1** provides an overview of the study design. All subjects were instructed and weight stabilized on an AHA Step 1 diet (1) for 1-2 months, after which baseline (time 0) measurements of body weight, waist circumference, resting BP, fasting lipids, glucose and inflammatory proteins were measured following a 12-hour overnight fast as previously described (13,21). On separate days after a 12- hour overnight fast, BART was performed to measure flow-mediated dilation (FMD) (21). All subjects signed informed consent and the protocol was approved by the Institutional Review Boards of the University of Maryland School of Medicine and the Baltimore Veterans Affairs Medical Center.

Dietary Instruction and Randomization to high-oleic Sunflower or Safflower oil based muffins

During the AHA Step 1 stabilization diet and at baseline, energy intake was composed of 45-50% carbohydrates, 15-20% protein and 30-35% of fat divided approximately equally between SFA, MUFA and PUFA. Following baseline measurements, subjects were randomized using a 1:1 assignment ratio to either a hypocaloric MUFA or PUFA enriched diet for 6 months aimed at reducing energy intake by ~300 kcal/day. While the relative percentages of CHO, fat and protein were kept constant, the SFA content was reduced in both groups from ~30% to ~25% of total fat intake and replaced with either MUFA or PUFA. Dietary assignment included daily consumption of 3 *MUFA* (high-oleic sunflower oil) or *PUFA* (safflower oil) enriched muffins. Each 3.5-ounce muffin contained 275 calories; high-oleic sunflower oil muffins contained 10.3 gram MUFA, 0.7 gram PUFA and 1.4 gram SFA and safflower oil muffins contained 9.2 gram PUFA, 2 gram MUFA and 1 gram SFA. All muffins were prepared in the metabolic kitchen of the USDA (Beltsville,

MD) and kept frozen in a canister until use. Participants met with a registered dietitian (RD) weekly for the first four months and then biweekly to collect a fresh supply of muffins and reinforce individual dietary and weight loss recommendations. Participants were also asked to complete 7-day food records upon completion of baseline testing (immediately prior to the MUFA-PUFA intervention) and at the end of the 6 month MUFA-PUFA intervention. The dietary food records included the number of muffins consumed daily as well as consumption of other MUFA and PUFA containing foods. Energy and nutrient composition was assessed using Nutritionist Pro™ software.

MOVE! Program

At baseline, participants received a submaximal Bruce exercise stress test (22) was performed to evaluate cardiovascular safety for exercise and endurance, after which they were instructed by an exercise physiologist on the Veteran's Affairs based *MOVE*! Program. The *MOVE*! Program is a leisurely home-based walking program (23). During the 6-month intervention phase, subjects were encouraged to walk on their own at least three-days per week for 30-45 minutes. Following completion of the six-month MUFA or PUFA assignment, subjects were weight stabilized for ten days before repeat post-dietary testing.

Lipoprotein and Biochemical Analysis—Following an overnight fast, 30 mL of blood was collected by venipuncture into 2 tubes containing EDTA and centrifuged within 30 minutes at 4°C to separate plasma. Total cholesterol and TG concentrations were measured using a Hitachi 704 clinical chemistry analyzer (Boehringer Mannheim Diagnostics, Indianapolis, IN) with reagents supplied by the manufacturer (cholesterol/HP, cat. no. 816302; triglycerides/GPO, cat. no 816370). HDL-C was measured in the clear supernatant following a double precipitation with high-molecular weight dextran sulfate as previously described (24). Plasma samples were stored at –80°C for analysis of inflammatory biomarkers high sensitivity C-reactive protein (hs-CRP), interleukin-8 (IL-8) and tumor necrosis factor alpha (TNFα) using a Proinflammatory Panel V-Plex Kit (Meso Scale Diagnostics, Inc). Glucose levels were measured by a glucose oxidase method (Beckman Instruments, Fullerton, CA) and insulin by insulin specific double antibody radioimmunoassay using human insulin standards and tracer (Linco, St. Louis, MO) with baseline and post-intervention samples included in the same assay.

FMD Assessment—Subjects were instructed to be in a fasting state and not smoke or drink coffee for 12 or more hours prior to the study. The next morning, they were positioned on a stretcher bed in a temperature-controlled room designated for BART studies to measure FMD. An automatic blood pressure cuff was placed on the right arm for intermittent blood pressure and heart rate monitoring throughout the study. Electrodes were placed to monitor a one lead EKG from the ultrasound system. Another blood pressure cuff was placed on the subject's upper left arm well above the antecubital fossa. The brachial artery was imaged above the antecubital fossa in the longitudinal plane by continuous 2D gray-scale imaging using an 11 MHz ultrasound (HDI 5000 [Phillips, Andover, Massachusetts]) by a trained sonographer as previously described (21). The blood pressure cuff was inflated to 200 mm Hg and kept inflated for 5 minutes. Upon immediate release of the cuff, the brachial artery was imaged and Doppler assessment of the hyperemic velocity was recorded within 8

seconds followed by 2D imaging with maximum dilation occurring 1 minute after cuff release. Using longitudinal images, the boundaries for diameter measurement were calibrated manually at the lumen-intima interface. All images were captured on videotape and read in a blinded fashion.

Statistical Analyses—Baseline (following the baseline AHA diet and immediately prior to MUFA or PUFA assignment) comparisons of subjects randomized to MUFA vs. PUFA groups was performed with one-way ANOVA. The group changes (six-month value minus baseline) were computed and compared between groups using one-way ANOVA adjusted for the baseline value of the outcome measure and the change in weight that occurred during the six-month MUFA-PUFA intervention (change=group + baseline value + weight change). Results are presented as mean ± SEM. A two-tailed $p< 0.05$ was considered statistically significant. Statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, NC).

Results

Subjects

A total of 182 men and women were screened for the study and of the 60% who qualified (n=110) 20% dropped out during the AHA dietary baseline phase (n=88) and 44% (n=39) completed the 6-month dietary MUFA (n=23) or PUFA (n=16) intervention. The post-randomization attrition rate included unanticipated medical and family events (e.g., extended medical illness) and loss to followup. The study subjects, 60% were women and 79% were African-American were obese (mean BMI: 35.7 ± 0.9 kg/m^2, range, 22-47 kg/m^2) with a mean age of 60.9 ± 8.5 years (range: 38-76) for whom. Of medications affecting BART, only a small percentage received statins (MUFA, 26%; PUFA, 25%) or angiotensin-converting enzyme inhibitors (MUFA, 26%; PUFA, 19%) at baseline. Medications and dosage regimen remained stable throughout the 6-month study.

Dietary Compliance

As shown in **Table 1,** 34 of 39 participants completed 7-day dietary food records, providing the energy and macronutrient composition at baseline (time 0) and at completion of the 6 month MUFA or PUFA dietary intervention There were no significant differences between the 2 groups in total energy intake or in CHO, protein, total or saturated fat at baseline. Similarly, the change in these metabolic components over the 6-month intervention did not differ between groups. During the study, the proportion of SFA to total fat consumed was reduced in MUFA (29% to 26%; *P=0.08*) and PUFA assigned groups (28% to 25%; *P<0.01*). Reciprocally, there was a 46% increase in the MUFA/SFA ratio in the MUFA group (*P <0.0001*), while assignment to PUFA was associated with a 59% increase in PUFA/SFA intake (*P<0.005*). Not surprisingly, assignment to MUFA resulted in increased consumption of 18:1 oleate (*P<0.01*), whereas PUFA treatment was associated with greater intake of 18:2 linoleate (*P<0.01*) and α-tocopherol (*P<0.0001*). Because omega-3 fish oil capsule supplementation was not permitted by the subjects, there were no significant differences in the intake of marine-based 20:5 EPA (eicosapentanoic acid) and 22:6 DHA (docosahexanoic acid) between the groups.

Cardiometabolic Outcomes

The prevalence of MetS components at baseline was hypertension (90%), fasting plasma glucose ≥ 100 mg/dL (82%) or T2DM (51%), increased waist circumference (72%), low HDL-C (67%) and TG > 150 mg/dL (21%). Compared to baseline, reductions in body weight and waist circumference were observed following MUFA (−2.3±1 kg, *P=0.06*: −2.8 ±1 cm, *P=0.02*) and PUFA (−4.6± 2 kg, *P=0.002*: −5.8±2 cm, *P=0.001*) intervention. The MUFA group demonstrated borderline significant decreases in insulin (*P=0.06*) and HOMA-IR whereas PUFA intervention was also associated with significant reductions in TG (−30±18 mg/dL, *P=0.02*), systolic blood pressure (BP) (−7±3 mmHg, *P=0.01*), diastolic BP (DBP) (−4±2 mmHg, *P=0.01*) and improved FMD (regardless of whether the change was expressed in mm or as a percentage change) (**Table 2**). Analysis of covariance demonstrated that the beneficial effects of PUFA compared to the MUFA-enriched diet on TG (*P=0.04*), FMD (*P=0.04*) and DBP (*P=0.07*) persisted independent of weight loss. However, the effects of both diets on biomarkers of inflammation (hsCRP, IL-8 and TNFα) were highly variable, and between group differences did not reach statistical significance. Overall, 18% subjects converted from MetS to non-MetS status, but there were no differences in conversion between the PUFA (4 of 16, 25%) and MUFA (3 of 23, 13%) MUFA groups (p<0.42 Fisher's Exact test).

Discussion

Our randomized study in which MUFA and PUFA-enriched fatty acids were substituted for SFA represents, to our knowledge, the first comparative study demonstrating the statistically significant beneficial effects of PUFA compared to MUFA in treating two components of MetS (weight and TG), a favorable trend on a third component (DBP), and clear benefits to FMD. The positive results in PUFA vs. MUFA are contrary to our original hypothesis and the known beneficial effects of MUFA- enriched diets on metabolism (9, 18, 19). It is possible that the addition of weight loss and the *VA MOVE!* Program in our obese subjects with MetS and T2DM receiving the PUFA diet likely contributed to the favorable outcomes.

Prior studies that focused on strategies for weight loss (~5-7% of body weight) via diet with or without low-intensity physical activity showed improvements in MetS constituents (25-26). Conversely, a diet high in SFA worsens MetS components and is associated with impaired FMD (21). While not all SFAs (e.g., plant-based) are highly atherogenic, animal-derived SFAs (i.e., red meat) are associated with a 25% increased risk of CV events (27). Indeed, with few exceptions (28) replacement of SFA for unsaturated fat is associated with reduced CV risk (8). A pooled analysis of 11 cohort studies found a 13% reduced CV risk when PUFA was substituted for SFA (29). The current study shows that the dietary substitution of SFA with PUFA or MUFA is associated with a 6.5% absolute increase in FMD a magnitude of change that is considered highly significant (20).

Although the present study found MUFA-enrichment to be associated with a 13% conversion rate to non-MetS status, PUFA-enrichment exhibited a 25% conversion rate, primarily by reducing waist, TG and a non-statistically significant trend toward reducing BP. Even though not demonstrated in the current study, the anti-inflammatory actions of PUFAs to lower acute phase reactants and proinflammatory mediators, even in the absence of any

appreciable intake of marine-derived omega-3 fatty acids are potential mechanisms to reduce CVD risk in MetS and T2DM (30-31). The reduction in cytokine release from adipose tissue decreases adipocyte lipolysis and FFA levels (32) and is associated with increased PPARγ activity and insulin sensitivity, all of which could reduce TG production (33) in MetS. Nevertheless, these metabolic advantages of PUFA compared to MUFA intake are relatively modest, and to some extent consistent with weight loss serving as a relevant contributor to the observed metabolic benefits (34-35).

To exclude the possibility of differences in the palatability and thus differential adherence to the MUFA vs. PUFA intervention, we blindly pretested the taste of the muffins at the onset of the trial. In fact, participants reported that they enjoyed consuming the assigned muffins. A potential reason for the greater weight loss in PUFA than in MUFA subjects is suggested by greater increases in the anorexigenic hormone peptide YY after PUFA intake compared to MUFA or SFA (36). In addition to the 4.6% reduction in body weight, PUFA enrichment continued to be associated with improved FMD, TG and a trend toward reduced DBP compared to MUFA assignment, even after controlling for weight loss. The basis for these differences is unclear, but may in part be related to the relatively low SFA intake (8.8% of total energy), which we previously showed to be inversely related to FMD (21). Indeed, the magnitude of improvement in FMD following PUFA treatment is similar to previous BART studies evaluating pharmacologic interventions (e.g., statins, ACE-inhibitors) (20,37), and the recent demonstration of an inverse association between PUFA intake and CVD risk further supports the substitution of a PUFA- enriched diet in place of SFA and trans fats (38).

There are several strengths and limitations associated with our study. Strengths included the use of USDA produced MUFA and PUFA- enriched muffins. To avoid potential confounding due to initial metabolic state, we designed the study so that subjects were metabolically and weight stabilized on an AHA type-I diet prior to the MUFA or PUFA intervention. Another notable highlight was the high percentage of African American (79%) participants, a group that is commonly underrepresented in clinical studies. Moreover, the prior studies that included subjects of African descent were generally observational, employing food-frequency questionnaires rather than a randomized intervention clinical trial (39). Unfortunately, the group samples were too small for a race-specific analysis.

Study limitations include the high post-randomization dropout rate of 55%. The value is similar to recent studies which have had rates of 50-60% range over a 6-month outpatient nutrition study period (40-41). Despite the high dropout rate, there was good compliance across the study groups in meeting the nutritional goals of this clinical trial, as evidenced by the 88% completion rate of food records (i.e., 34 of 39 subjects). Another limitation is the use of food record recall to assess dietary intake, a metric far less sensitive than when all meals are prepared and distributed from a metabolic kitchen. While all muffins were prepared by the USDA, additional dietary recommendations of required MUFA or PUFA intake was individualized by the dietitian according to participant preferences and standardized between the two groups for intake. Overall, the food records, while variable, met the study requirements and the primary endpoints of the study, both of which were favorably influenced by the PUFA more than MUFA diet. Finally, there were several

dropouts who provided blood samples at their 6-month follow up visit but chose not to return for their follow-up BART study due to logistical reasons (e.g., transportation, scheduling).

Conclusion

The results of this small, randomized clinical trial suggest PUFA rather than MUFA may be the unsaturated fat of choice for caloric replacement of saturated fatty acids in obese middle-aged men and women with MetS who are already following an AHA type-I diet and who are trying to lose weight and improve their cardiovascular risk profile. Even though the diets were adhered to and there were no apparent differences in energy intake between groups according to the food records, controlled metabolic dietary studies would be needed in a larger study sample to confirm these preliminary results and determine the mechanisms underlying the observed PUFA-derived cardiometabolic benefits in patients with MetS.

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Acronyms

ACE	angiotensin converting enzyme
AHA	American Heart Association
ANOVA	analysis of variance
BART	brachial artery reactivity testing
CHO	carbohydrates
CVD	cardiovascular disease
DHA	docosahexanoic acid
DBP	diastolic blood pressure
EPA	eicosapentanoic acid
FFA	free fatty acids
FMD	flow mediated dilation
HDL-C	high density lipoprotein cholesterol
Hs-CRP	high sensitivity C-reactive protein
HTN	hypertension
IL-8	interleukin-8

LDL-C	low density lipoprotein cholesterol
MetS	metabolic syndrome
MUFA	monounsaturated fatty acids
MUFFIN	monounsaturated fat for dietary management in the metabolic syndrome
NORC	Nutrition Obesity Research Center
PPAR-γ	peroxisome proliferator-activated receptor gamma
PUFA	polyunsaturated fatty acids
RD	registered dietitian
SBP	systolic blood pressure
SFA	saturated fatty acids
TG	triglycerides
T2DM	type 2 diabetes mellitus
TNFα	tumor necrosis factor alpha
WL	weight loss

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Highlights

- Compared to baseline, a PUFA or MUFA enriched diet was associated with weight loss.
- PUFA intervention was associated with greater reductions in TG, BP and FMD than MUFA.
- PUFA may be the fat of choice to reduce cardiometabolic risk in subjects with MetS.

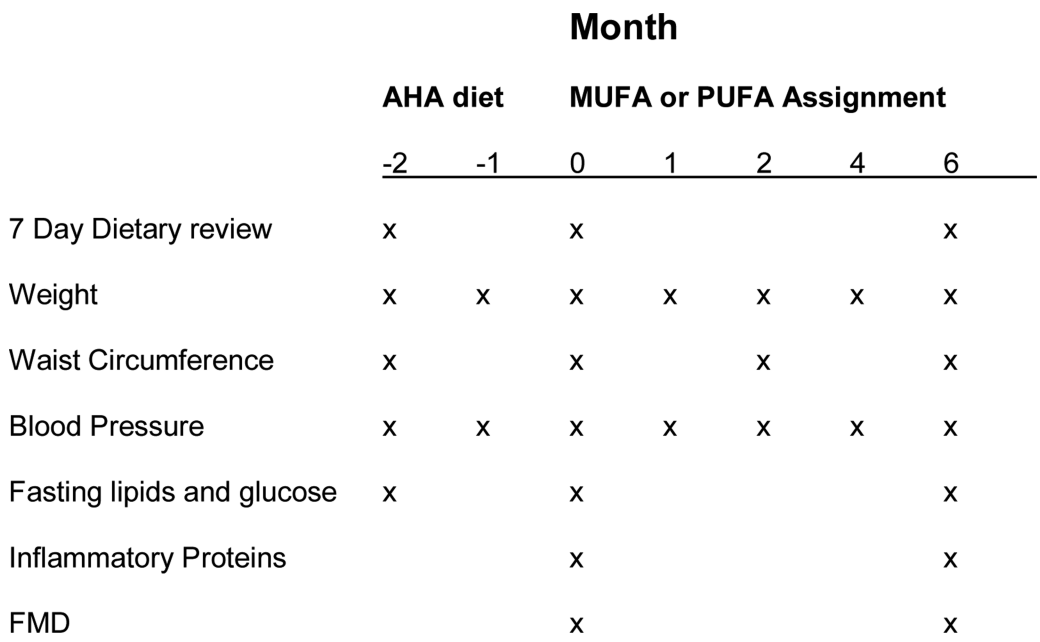

Figure 1.
Overview of study design prior to and following assignment to a MUFA or PUFA enriched diet

Table 1

Mean Energy and Nutrient Composition (+/− SE) at Baseline and after Dietary Intervention based on dietary records in MUFA (n=19) and PUFA (n=15) subjects

	Baseline	% *	6 months	% *	P value	
					Baseline-6 mo	MUFA vs. PUFA
KCAL						
MUFA	1657 (78.3)		1638 (61.4)		0.83	
PUFA	1649 (122.7)		1551 (87.1)		0.32	0.53
CHO (grams)						
MUFA	197.0 (13.0)	***47%***	171.6 (10.9)	***42%***	0.01	
PUFA	203.7 (17.2)	***49%***	189.5 (11.6)	***48%***	0.42	0.57
Protein (grams)						
MUFA	75.0 (4.2)	***18%***	77.9 (5.5)	***19%***	0.69	
PUFA	77.4 (5.6)	***19%***	67.3 (6.1)	***17%***	0.15	0.19
Total Fat (grams)						
MUFA	64.7 (3.9)	***35%***	69.4 (3.5)	***38%***	0.36	
PUFA	60.1 (6.0)	***33%***	61.4 (4.2)	***35%***	0.78	0.63
Sat Fat (grams)						
MUFA	18.7 (1.6)	***10%***	18.4 (1.4)	***10.1%***	0.84	
PUFA	17.4 (2.1)	***9.4%***	15.1 (1.2)	***8.8%***	0.19	0.44
18:1 (grams)						
MUFA	17.0 (1.5)		24.8 (1.8)		<0.01	
PUFA	14.4 (1.7)		13.1 (1.5)		0.37	<0.001
18:2 (grams)						
MUFA	10.7 (0.8)		9.6 (0.9)		0.35	
PUFA	10.1 (1.7)		16.9 (1.2)		<0.01	<0.001
20:5 (grams)						
MUFA	0.10 (0.02)		0.07 (0.04)		0.37	
PUFA	0.05 (0.02)		0.10 (0.07)		0.44	0.28
22:6 (grams)						
MUFA	0.21 (0.05)		0.10 (0.04)		<0.05	
PUFA	0.10 (0.03)		0.15 (0.08)		0.52	0.11
α-tocopherol (IU)						
MUFA	5.5 (1.0)		6.8 (0.8)		0.15	
PUFA	4.6 (0.4)		9.5 (0.8)		<0.0001	<0.01
SFA/total fat (%)						
MUFA	29 (11)		26 (1)		0.08	
PUFA	28 (1)		25 (1)		<0.01	0.38
Mono fat/sat fat (%)						
MUFA	114 (8)		167 (10)	** ***46%***	<0.0001	0.001
PUFA	104 (10)		104 (6)		0.95	
Poly fat/sat fat (%)						

	Baseline	% *	6 months	% *	P value	
					Baseline-6 mo	MUFA vs. PUFA
MUFA	81 (8)		67 (5)		0.11	<0.0005
PUFA	83 (12)		132 (11)	** 59%	<0.005	

* Percentage of total energy intake

** Percentage increase between baseline and 6 months

Table 2

Effect of 6 months of MUFA vs. PUFA diet on metabolic parameters and markers of inflammation

	MUFA					PUFA					Between Groups	
		Month		Within group			Month		Within group			
Outcome	N	0	6	Change	P	N	0	6	Change	P	P*	P**
		Mean(SE)	Mean(SE)	Mean(SE)			Mean(SE)	Mean(SE)	Mean(SE)			
Weight (kg)	23	106(4)	104(4)	−2.3(1)	0.06	16	103(3)	98(3)	−4.6(2)	**0.002**	0.2	N/A
Cholesterol (mg/dl)	23	166(9)	175(8)	9(5)	0.22	16	172(11)	170(14)	−1(11)	0.88	0.37	0.48
LDL-C (mg/dl)	23	100(7)	103(6)	2(3)	0.67	16	97(10)	101(12)	4(9)	0.6	0.89	0.92
HDL-C (mg/dl)	23	46(3)	48(3)	2(1)	0.23	16	48(4)	49(4)	2(2)	0.41	0.89	0.85
Triglucerides (mg/dl)	23	109(8)	114(9)	6(5)	0.6	16	135(21)	105(14)	−30(18)	**0.02**	**0.04**	**0.01**
Fasting glucose (mg/dl)	23	116(4)	119(4)	2(5)	0.69	15	111(5)	112(6)	1(3)	0.81	0.95	0.83
Insulin (UNITS)	22	99(10)	83(8)	−16(8)	0.06	14	83(9)	76(15)	−7(12)	0.52	0.48	0.87
HOMA (UNITS)	21	4.3 (0.5)	3.5(0.4)	−0.8(0.5)	0.1	13	3.1(0.4)	3.2(0.8)	0.1(0.5)	0.94	0.28	0.83
SBP (mmHg)	23	128(2)	125(2)	−3(2)	0.15	16	128(2)	121(2)	−7(3)	**0.01**	0.26	0.15
DBP (mm Hg)	23	74(1)	73(1)	−1(1)	0.38	16	72(2)	68(1)	−4(2)	**0.01**	0.15	0.07
FMD (mm)	22	2.5 (0.4)	2.5(0.3)	0(0.3)	1	12	1.9(0.5)	3.6(0.5)	1.7(0.5)	**0.001**	**0.006**	**0.04**
FMD (%)	22	8.6(1.2)	9.6(1.0)	1(1.1)	0.42	12	7.1(1.8)	13.6(2)	7.1(1.8)	**0.0001**	**0.004**	**0.04**
hsCRP (UNITS)	22	5.9(1.8)	5.1(1.6)	−0.8(1.2)	0.48	16	4.1(0.9)	4.8(1.0)	0.7(0.9)	0.59	0.39	0.77
IL-8 (UNITS)	22	6.6(0.6)	7.3(0.7)	0.6(0.4)	0.25	16	7.2(0.9)	7.9(0.8)	0.7(0.8)	0.27	0.92	0.98
TNFα (UNITS)	22	2.3(0.2)	2.4(0.2)	0.1(0.1)	0.39	16	1.9(0.1)	2.0(0.2)	0.2(0.1)	0.05	0.33	0.45

*Unadjusted p value

**Adjusted for initial value of outcome measure and change in weight during six-month MUFA or PUFA intervention.